

**Definition**

Diabetes mellitus is the name given to a heterogeneous group of disorders that have in common abnormal glucose tolerance. The classification given here (Table 136.1) is based on etiologic differences between these disorders rather than the formerly used phenomenologic classification.

Insulin-dependent diabetes mellitus (IDDM) or type I diabetes, formerly called juvenile-onset diabetes, is characterized by absolute dependency on exogenous insulin. About 10% of all people with diabetes have this type.

Non-insulin-dependent diabetes mellitus (NIDDM) or type II diabetes, formerly referred to as adult-onset, maturity-onset, is characterized by gradual onset and hyperglycemia but no tendency to ketoacidosis except under extraordinary stress. People with NIDDM may take insulin

to control hyperglycemia, but it is not absolutely required. About 60 to 70% of people with NIDDM are obese, and this type is sometimes subdivided into obese and nonobese categories. Eighty-five to 90% of all people with diabetes have this type.

Maturity-onset diabetes in the young (MODY) differs from NIDDM in that it has a clearly defined autosomal dominant inheritance pattern. The hyperglycemia in this type is generally quite mild. MODY is also characterized by a decreased frequency of the long-term complications of diabetes.

Diabetes due to abnormalities in the amino acid sequence of insulin or abnormalities in cleavage from proinsulin causing decreased insulin action have been referred to as insulinopathies, in a manner analogous to the hemoglobinopathies. The prevalence of these abnormalities has not been established.

At least three types of diabetes have been found in association with the dermatologic disorder acanthosis nigricans. These three types are associated with severe resistance to the action of insulin due to an abnormal insulin receptor (type A), antibodies to the insulin receptor (type B) or post-receptor abnormalities (type C).

A number of congenital syndromes are associated with abnormal glucose tolerance, but the mechanisms responsible for the disordered carbohydrate metabolism are mostly unknown.

Diabetes may be secondary, as a result of direct ablation of the beta cells in association with pancreatitis, pancreatectomy, or hemochromatosis.

A separate category has been designated as gestational diabetes and refers to women whose diabetes first becomes manifest during pregnancy. Although the diabetes normally resolves upon delivery, over the following years over 50% of such women subsequently relapse into overt NIDDM.

The criteria for the varying degrees of impairment in glucose tolerance are given in Table 136.2. These criteria are used for the diagnosis of diabetes mellitus but not for the type of diabetes.

**Table 136.1**  
Types of Diabetes Mellitus

Type	Other names used
Insulin-dependent diabetes mellitus (IDDM)	Type I, juvenile-onset
Non-insulin-dependent diabetes mellitus (NIDDM)	Type II, adult-onset, maturity-onset
Maturity-onset diabetes in the young (MODY)	Mason-type diabetes
Abnormal insulin structure	Insulinopathies
Insulin resistance associated with acanthosis nigricans	
Diabetes associated with congenital disorders	
Secondary diabetes	
Gestational diabetes	

**Table 136.2**  
Categories of Glucose Tolerance Impairment in Nonpregnant Adults

Category	Fasting (mg/dl)	½ h, 1 h, 1½ h OGTT value (mg/dl)	2 h OGTT value (mg/dl)
Normal	<115*	<200	<140
Impaired glucose tolerance	<140	≥200	140–200
Diabetes mellitus	>140*	≥200	≥200

Source: Adapted from the National Diabetes Data Group categorization (National Diabetes Data Group, 1979).

\*All values assume venous plasma glucose measured.

†Diagnosis of diabetes mellitus can be made if FBC > 140 on 2 separate days. If FBC < 140, then both 2 h sample and some other value between the fasting and 2 h value must both be ≥200 mg/dl.

Three types of acute complications generally occur: severe hyperglycemia associated with a hyperosmolar, non-ketotic state; severe hyperglycemia associated with ketoacidosis; and hypoglycemia.

The chronic complications are generally classified into vascular and nonvascular. Macrovascular complications are caused by large vessel disease and the complications relate to the vascular system involved (e.g., cerebrovascular, coronary artery, and peripheral vascular disease). Microvascular complications are caused by small vessel disease and include retinopathy, renal glomerular disease (Kimmelstiel-Wilson disease), some of the neuropathies (mononeuropathies), and possibly cardiac and other small vessels. Nonvascular complications include cataracts and polyneuropathy, both peripheral and autonomic.

## Technique

The history can conceptually be divided into several sections: classification of type of diabetes; delineation of any complications of diabetes; assessment of usual control and especially recent control of the diabetes; mode of therapy, including diet, exercise, oral hypoglycemic agents, and insulin; and medications or conditions that can have an impact on the control of diabetes.

The type of diabetes is usually easy to classify. Ketoacidosis at onset or with moderate stress usually indicates IDDM. Insulin use *per se* does not differentiate between IDDM and NIDDM, as patients with the latter may be using insulin to control hyperglycemia. One the other hand, lack of the requirement for insulin effectively excludes IDDM. In many patients, especially those with onset of disease in their 20s and 30s, it may be difficult to classify them if they have never had ketoacidosis.

Patients with MODY have a strong family history of diabetes that should display an autosomal dominant mode. The insulin receptor disorders are characterized by acanthosis nigricans, which may be detected only on examination. For patients with secondary diabetes, a history of pancreatitis and/or pancreatectomy is usually obtainable. Patients with hemochromatosis will usually display the characteristic hepatomegaly and bronzing of their skin; they are often hypogonadal.

The frequency of episodes of severe hyperglycemia may be a clue to underlying medical conditions, such as recurrent urinary tract infections or psychologic disorders. Those patients, said to be "brittle," usually have some underlying reasons for their brittleness. Frequent hypoglycemic reactions are usually the result of erratic timing of meals and/or exercise that does not match the timing of insulin injections. Critical parts of the history in detecting the presence of hypoglycemia reactions at night during sleep are the presence of nightmares, excessive perspiration, and waking up in the morning with a headache. Often the urine will show morning ketones after a nocturnal hypoglycemic episode. Some patients with long-standing IDDM lose many of the warning symptoms characteristic of hypoglycemia (e.g., tremor, perspiration, anxiety). Such patients may go from feeling normal to unconsciousness within a few minutes. Therefore, it is necessary to ask what typical symptoms patients have from a hypoglycemia reaction. Hypoglycemia rarely occurs in patients taking oral hypoglycemic agents, but when it does, it may be prolonged and may require inpatient treatment. Rarely, fasting hyperglycemia may in-

dicate the development of an insulinoma, for which patients with diabetes are at increased risk.

Patients may or may not be aware of any chronic complications. A slow, gradual decrease in vision may indicate presence of a cataract, especially in older patients. A more recent blurring of vision may simply indicate lens swelling and poor control. Sudden loss of vision is of more concern and indicates need for rapid ophthalmologic consultation. A sudden loss of vision may result from hemorrhage, a retinal detachment, or vascular disease. Sudden onset of diplopia or ptosis may be indicative of cranial nerve infarct, but other causes need exclusion. Bell's palsy is also more frequent with diabetes.

Loss of strength and speech or other neurologic symptoms may be secondary to cerebrovascular disease, usually of the thrombotic type. In patients with occlusive coronary artery disease there commonly is no pain with myocardial infarction. Therefore, the sudden onset of dyspnea, peripheral edema, and other symptoms of congestive heart failure may be indicative of a recent infarction.

Nephropathy is often silent until advanced stages when patients may present with edema and nephrotic syndrome. Hypertension may reflect developing nephropathy. Historical review, however, may elicit a previous history of previous physicians having noticed proteinuria. Uncommonly, renal failure may present as an increase in hypoglycemic reactions caused by loss of the kidney component of insulin degradation.

Early peripheral neuropathy is frequently asymptomatic. In later stages, patients may complain of numbness or burning pains in the feet. These neuropathic findings may also be present in the hands, and patients frequently complain of dropping things. As the neuropathy progresses, the symptoms ascend in a stocking-glove fashion. The carpal tunnel syndrome is more frequent in patients with diabetes, and its characteristic symptoms may be confused with diabetic neuropathy. Muscle weakness and atrophy may be present with diabetic neuropathic amyotrophy, especially in the hands.

Peripheral neuropathy may cause the development of foot ulcers because the patient does not feel the discomfort of poorly fitting shoes or a pebble. Questioning as to evidence of redness or skin breakdown may serve to prevent future problems.

The various types of autonomic neuropathy can be particularly bothersome. Cardiac plus peripheral vascular autonomic neuropathy may cause orthostatic hypotension and lightheadedness. Gastrointestinal autonomic neuropathy may cause delayed gastric emptying so that patients may develop early satiety and vomiting of undigested food. Such patients may also get hyperglycemic because of mismatching of insulin action and the timing of nutrient absorption from the intestine. Intestinal autonomic neuropathy may also cause erratic peristalsis, nocturnal diarrhea being a common complaint. Rarely, such patients may develop bacterial overgrowth and steatorrhea, with its symptoms of foul-smelling, floating, greasy stools.

Genitourinary neuropathy is a common cause of impotence in diabetic men, although vascular disease may also be a cause. Neuropathic or vascular impotence is characterized by absence of nocturnal and morning erections but intact libido. There are several varieties of bladder neuropathy, and an early sign may be recurrent urinary tract infections secondary to failure of complete bladder emptying.

Symptoms of new onset or poor control of diabetes in-

clude polyuria, polydipsia, polyphagia, weight loss, fatigue, and vaginal candida infections. Most patients with previously diagnosed disease monitor their diabetes by either self-monitoring of blood glucose levels or urine glucose testing. These tests may be assessed for the degree of control. Evidence of a recent decrease in glycemic control may be a clue to an underlying infection or inflammatory disorder.

The various modes of therapy used by the patients are important. Assessment of adherence to diet or compliance with an insulin regimen may reveal why control has worsened or hypoglycemic reactions occur. Remember the rather large interindividual variation in insulin time of action in this regard. The pattern of insulin site rotation may be important, as exercise shortly after injection of insulin into an exercising limb has been shown to affect insulin absorption dramatically.

In patients taking the older oral hypoglycemic agents, symptoms of flushing and dizziness may indicate an Antabuse-like reaction to alcohol. These drugs may also uncommonly cause cholestatic jaundice. Chlorpropamide use may occasionally result in the syndrome of inappropriate antidiuretic hormone (SIADH) secretion so that patients may present with altered consciousness.

Other medications may also affect the diabetes. Propranolol and other nonselective beta blockers may cause both a worsening of glucose tolerance and also a decrease in the ability to recover from hypoglycemia. Furthermore, these drugs may block some of the adrenergic warning symptoms of hypoglycemia (e.g., palpitations or tremor), resulting in more profound hypoglycemia with loss of consciousness. Thiazide diuretics, estrogens, and phenytoin may worsen glucose tolerance as well.

## Basic Science

The current classification given of diabetes is based on etiology. Based on proper classification of patients, future epidemiologic studies may afford better insights into the pathogenesis and prognosis of the types of diabetes and their complications.

The autoimmune etiology for IDDM is well established and is quite different from the etiology of NIDDM. Although the etiology of NIDDM is not well understood, it is clear that this disorder is characterized by resistance to the action of insulin, inability of the islets to secrete enough insulin to overcome the insulin resistance, and overproduction of glucose by the liver.

The long-term complications of diabetes are likely caused by the abnormal metabolic milieu. Although some studies suggest that long-term complications may be ameliorated in some cases by intensive management that has the aim of restoring normoglycemia, this has not been proven. Whether

the long-term complications can be prevented remains to be seen. It is also clear that such intensive management results in a significantly greater frequency of hypoglycemic reactions.

The links postulated to occur between the complications of diabetes and the abnormal metabolism include accumulation of polyols in tissues, glycosylation of structural proteins, and lowering of high-density lipoproteins (HDL) and elevation of low-density lipoproteins (LDL).

## Clinical Significance

Diabetes mellitus affects more than 12 million individuals in the United States. It is the third cause of death by disease and the leading cause of new blindness in adults aged 20–74. Compared to the general population, patients with diabetes have a twofold increase in the risk for heart disease and stroke, and a 17-fold increase in the risk for renal failure. Diabetes accounts for 50% of all leg amputations performed annually. Thus diabetes is a major public health problem resulting in over 2 million hospitalizations per year and causing an annual estimated \$20 billion drain on the U.S. economy. Most of this cost is due to the long-term complications of the disease. Any steps that clinicians can take to prevent or postpone these complications will have far-reaching benefits.

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